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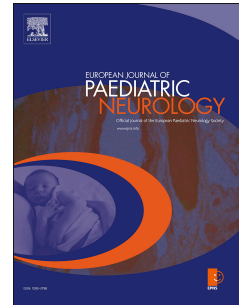
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Immune-mediated neurological syndromes: old meets new

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The discovery of a range of brain and glial directed autoantibodies has allowed clinicians to associate these antibodies to specific neurological syndromes;⁽¹⁾ and have additionally started to unify past and present clinically identical neurological syndromes. For example, the intriguing polysymptomatic eponymous Sébire encephalitis is now acknowledged by many to be anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis.⁽²⁾ 50 years after Lord Brain first described Hashimoto's Encephalopathy (HE), a disorder characterized by diverse neurological dysfunction with associated elevated anti-thyroid antibodies, Chen et al. describe a child with an inflammatory encephalopathy in whom both anti-thyroid and myelin oligodendrocyte glycoprotein (MOG) autoantibodies were identified.⁽³⁾

Whilst there has been agreement amongst clinicians on the existence of a neurologic syndrome associated with thyroid antibodies; and its clinical response to steroid therapy alongside association with other autoimmune diseases suggesting an immune mediated central nervous system disorder, there remains significant doubt of the pathogenic role of thyroid antibodies.⁽⁴⁾ Similarly, although MOG antibody appear to mediate clinical and radiological phenotype of demyelination that is distinguishable from multiple sclerosis,⁽⁵⁾ the precise mechanistic effects of antibodies are not resolved. Nonetheless, it is plausible that MOG, expressed in the outermost lamella of the myelin sheath, may either be a primary target of autoimmunity or may become exposed in any brain inflammation, particularly in those in whom myelin inflammation is ongoing. Thus, the main clinical question this child with a neurological syndrome and two antibodies identified is if the patient may have HE and MOG-associated brain inflammation concurrently or either HE or MOG associated brain inflammation with the respective other antibody not contributing to the neurologic syndrome.

The co-occurrence of auto-immune syndromes in patients is recognised and may target multi-organs or a single organ in multiple ways. Examples of brain directed autoimmunity co-occurring with systemic auto-immunity, as has been proposed in this case, and/or across a timeline are reported and would not be novel to clinicians. Importantly, we are starting to recognise that some co-occurrence may cluster more

frequently such as myasthenia gravis with neuromyelitis optica;⁽⁶⁾ or more specifically, MOG-antibody associated demyelination syndrome that may occur before, during or after anti-NMDAR encephalitis.⁽⁷⁾

The specificity of thyroid antibodies in predicting a neurological syndrome is limited as these autoantibodies are frequently also present in the general population without thyroid associated disease.⁽⁴⁾ A positive thyroid auto-antibody in the presence of encephalopathy may lead to the clinical diagnosis of HE, potentially in the context of a yet to be tested or identified pathogenic brain directed autoimmunity. The case reported by Chen et al⁽³⁾, alongside previously reported cases of HE sharing very distinct phenotypic similarity to cases of anti-MOG antibody associated demyelination, as reviewed by the authors, raises the important question if a subset of cases of HE are actually MOG antibody mediated disease.

Future identification of other neuronal surface antibodies are likely to define the precise target of autoimmunity in other previously recognised neurological syndromes. Importantly, care still needs to be given to establishing the clinical relevance and treatment implications of identification of these antibodies, including MOG antibodies.

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